

ATTORNEY DOCKET NO. 22000.0110U2

What is claimed is:

1. A method of enhancing the activity of Cyp 4A14 by administering an agent that enhances the activity of Cyp 4A14.
2. A method of inhibiting the activity of Cyp 4A14 by administering an agent that inhibits the activity of Cyp 4A14.
3. A method of inhibiting the activity of testosterone by administering an agent that enhances the activity of Cyp 4A14.
4. A method of enhancing the activity of testosterone by administering an agent that inhibits the activity of Cyp 4A14.
5. A method of enhancing the activity of Cyp 4A12 by administering an agent that enhances the activity of Cyp 4A12.
6. A method of inhibiting the activity of Cyp 4A12 by administering an agent that inhibits the activity of Cyp 4A12.
7. A method of inhibiting the activity of Cyp 4A12 by administering an agent that inhibits the activity of testosterone.
8. A method of enhancing the activity of Cyp 4A12 by administering an agent that enhances the activity of testosterone.
9. A method of enhancing the activity of Cyp 4A12 by administering an agent that inhibits the activity of Cyp 4A14.

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10. A method of inhibiting the activity of Cyp 4A12 by administering an agent that enhances the activity of Cyp 4A14.

11. A method of enhancing the activity of human Cyp 4A11 by administering an agent that enhances the activity of human Cyp 4A11.

12. A method of inhibiting the activity of human Cyp 4A11 by administering an agent that inhibits the activity of human Cyp 4A11.

13. A method of enhancing the activity of human Cyp 4A11 by administering an agent that inhibits the activity of Cyp 4A14.

14. A method of inhibiting the activity of human Cyp 4A11 by administering an agent that enhances the activity of Cyp 4A14.

15. A method of inhibiting the activity of human Cyp 4A11 by administering an agent that inhibits the activity of testosterone.

16. A method of enhancing the activity of human Cyp 4A11 by administering an agent that enhances the activity of testosterone.

17. A method of enhancing the activity of human Cyp 4A11 by administering an agent that inhibits the activity of Cyp 4A14.

18. A method of inhibiting the activity of human Cyp 4A11 by administering an agent that enhances the activity of Cyp 4A14.

19. A method of identifying an agent capable of enhancing the activity of Cyp 4A14, comprising contacting Cyp 4A14 with a test agent, and determining if the activity of Cyp 4A14 is enhanced as compared to the activity of uncontacted Cyp

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4A14, whereby an increase in Cyp4A14 activity indicates that the test agent is capable of enhancing the activity of Cyp 4A14.

20. A method of identifying an agent capable of inhibiting the activity of Cyp 4A14, comprising contacting Cyp 4A14 with a test agent, and determining if the activity of Cyp 4A14 is inhibited as compared to the activity of uncontacted Cyp 4A14, whereby a decrease in Cyp4A14 activity indicates that the test agent is capable of inhibiting the activity of Cyp 4A14.

21. A method of identifying an agent capable of enhancing the activity of Cyp 4A12, comprising contacting Cyp 4A12 with a test agent, and determining if the activity of Cyp 4A12 is enhanced as compared to the activity of uncontacted Cyp 4A12, whereby an increase in Cyp4A12 activity indicates that the test agent is capable of enhancing the activity of Cyp 4A12.

22. A method of identifying an agent capable of inhibiting the activity of Cyp 4A12, comprising contacting Cyp 4A12 with a test agent, and determining if the activity of Cyp 4A12 is inhibited as compared to the activity of uncontacted Cyp 4A12, whereby a decrease in Cyp4A12 activity indicates that the test agent is capable of inhibiting the activity of Cyp 4A12.

23. A method of screening for an agent capable of inhibiting the activating effect of testosterone on the activity of Cyp 4A12, comprising contacting Cyp 4A12 with a test agent in the presence of testosterone, and determining if the activity of Cyp 4A12 is inhibited as compared to the activity of Cyp 4A12 in the presence of testosterone but which has not been contacted with the test agent, whereby a decrease in Cyp 4A12 activity indicates that the test agent is capable of inhibiting the activating effect of testosterone on the activity of Cyp 4A12.

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24. A method of screening for an agent capable of enhancing the activating effect of testosterone on the activity of Cyp 4A12, comprising contacting Cyp 4A12 with a test agent in the presence of testosterone, and determining if the activity of Cyp 4A12 is enhanced as compared to the activity of Cyp 4A12 in the presence of testosterone but which has not been contacted with the test agent, whereby an increase in Cyp4A12 activity indicates that the test agent is capable of enhancing the activating effect of testosterone on the activity of Cyp 4A12.

25. A method of screening for an agent capable of inhibiting the activating effect of testosterone on the activity of human Cyp 4A11, comprising contacting human Cyp 4A11 with a test agent in the presence of testosterone, and determining if the activity of human Cyp 4A11 is inhibited as compared to the activity of human Cyp 4A11 in the presence of testosterone but which has not been contacted with the test agent, whereby a decrease in human Cyp 4A11 activity indicates that the test agent is capable of inhibiting the activating effect of testosterone on the activity of human Cyp 4A11.

26. A method of screening for an agent capable of enhancing the activating effect of testosterone on the activity of human Cyp 4A11, comprising contacting human Cyp 4A11 with a test agent in the presence of testosterone, and determining if the activity of human Cyp 4A11 is enhanced as compared to the activity of human Cyp 4A11 in the presence of testosterone but which has not been contacted with the test agent, whereby an increase in human Cyp 4A11 activity indicates that the test agent is capable of enhancing the activating effect of testosterone on the activity of human Cyp 4A11.

27. A non-human transgenic mammal comprising a gene encoding murine Cyp 4A14 which has been inactivated or completely deleted.

28. The non-human transgenic mammal of claim 27, wherein the non-human transgenic mammal is a mouse.

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29. A non-human transgenic mammal comprising a gene encoding murine Cyp 4A12 which has been inactivated.

30. The non-human transgenic mammal of claim 29, wherein the non-human transgenic mammal is a mouse.

31. The non-human transgenic mouse of claim 28, wherein the endogenous murine Cyp 4A12 gene has also been inactivated or completely deleted, and wherein a copy of the human Cyp 4A11 gene has been introduced into the genome of the mouse and is active in the mouse.

32. The mouse of claim 31, wherein the human Cyp 4A11 gene has been inactivated.

33. A method of identifying an agent capable of reducing hypertension, comprising administering a test agent to the mouse of claim 28, and comparing the blood pressure of the mouse to the blood pressure of a mouse of claim 28 to which the test agent has not been administered, wherein a lower blood pressure in the first mouse as compared to the second mouse indicates that the test agent is capable of reducing hypertension.

34. A method of identifying an agent capable of reducing hypertension, comprising administering a test agent to the mouse of claim 31, and comparing the blood pressure of the mouse to the blood pressure of a mouse of claim 31 to which the test agent has not been administered, wherein a lower blood pressure in the first mouse as compared to the second mouse indicates that the test agent is capable of reducing hypertension.

35. A method of treating hypertension in an individual comprising inhibiting testosterone activity in the individual.

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36. A method of treating hypertension in an individual comprising enhancing Cyp 4A14 activity in the individual.

37. A method of treating hypertension in an individual comprising inhibiting Cyp4A11 activity in the individual.

38. A method of treating hypertension in an individual comprising inhibiting testosterone activity by enhancing 4A14 activity in the individual.

39. A method of identifying a subject having an increased susceptibility for developing hypertension, comprising detecting a mutant Cyp 4A11 polypeptide or a mutated Cyp 4A11 nucleic acid in the subject, thereby identifying a subject having an increased susceptibility for developing hypertension.

40. The method of claim 39, wherein the mutated nucleic acid encodes Cyp 4A11/W126→R.

41. The method of claim 39, wherein the mutated nucleic acid encodes Cyp 4A11/R231→C.

42. The method of claim 39, wherein the mutated nucleic acid encodes Cyp 4A11/M369→R.

43. The method of claim 39, wherein the mutated nucleic acid encodes Cyp 4A11/L509→F.